DEPARTMENT OF MEDICINE PROPOSAL

to

STANFORD UNIVERSITY

to establish

AN INSTITUTE OF BIOLOGICAL AND CLINICAL INVESTIGATION

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INTRODUCTION

We propose to develop a long-term, continuous collaboration with the chemical, pharmaceutical and engineering industries with which academic medicine and the University share common interests.

The purpose of the collaboration is five-fold:

1. To allow the Department of Medicine and the School of Medicine to find alternative sources of income and to decrease their dependence on the uncertainty of federal research support and non-expandable clinical income.

2. To provide a vehicle for expediting the orderly transfer of new pharmacologic developments and biological observations from the University to industry for clinical application.

3. To provide faculty with access to areas of science not available in the Medical School, and conversely to assist industry in tapping academic talent working on the frontiers of advancing science.

4. To provide industry, which lacks clinical facilities, the full capability of clinical and research strategies of clinical investigation.

5. To develop a model for demonstrating the capability and importance of industry/university collaboration to the support of academic functions for the benefit of both and of society in general.

Collaboration with industry will be businesslike with research contracts made by both parties and involving the commitment of the entire Department of Medicine faculty who have been on the staff for more than three years. Eventually participants may join from the other departments of the Medical School and the University. We do not intend to use the Institute to expand the faculty in the Department of Medicine. Rather we intend to use the

resource to allow us to develop young faculty to replace retiring academicians, instead of replacing them with older faculty whose attractiveness to academics and outside funding agencies is already established.

WHY UNIVERSITY/INDUSTRY COLLABORATION?

The Special Needs of Industry

Successful collaborations between industry and academia are a matter of record, but these have occurred notably abroad.

In the 1930's the work with the Karolinska Institute was underwritten by pharmaceutical companies and has continued successfully to the present time. In Switzerland collaboration between industry and the universities has resulted in the former underwriting the enormous costs of academic programs. In England there have been a few successful long-range relationships between selected universities and a number of pharmaceutical companies. No university/industry collaboration worthy of note has occurred in the United States. The only exception is the development of technology licensing efforts to protect patentable inventions of individual faculty members, with income shared by the universities and the inventors. The leading examples of this are the University of Wisconsin and the University of Michigan.

There are important benefits in collaborating with industry because this area is largely unexplored. What collaborations have been notably successful seem to have occurred between few companies and few universities. ICI in England has done most of its development work in academic settings. Smith, Kline &French has used academicians to develop the H2 receptor blockers. All agreements have been between industry and individual faculty members and are not notable for their value to academic interests as a whole.

Ad hoc relationships involving single faculty members working with industry have very definite drawbacks. Neither industry nor the faculty members are very firmly committed in terms of the depth of the advice given or its consequences. And these ad hoc relationships have often not resulted in benefit to more than the faculty members involved or to more than a minority of the interests of the company. Frequently fruitful projects remain incomplete because artificial barriers to collaboration are created by the ad hoc agreements. That is, faculty members may not be at liberty to collaborate on the implications of an unanticipated finding because of the restrictions of the original agreements.

The Special Needs of Academic Medicine

The Stanford University School of Medicine is definitely vulnerable by its substantial dependence on the federal government for underwriting its three major functions. Government has made it clear that it will be reducing its level of support of training, research and tertiary care. The elimination of capitation funds in next year's federal budget indicates the reduced governmental interest towards teaching medical students. A nineteen percent decrease in three years, in constant dollars for fundamental research supported by the National Institutes of Health, indicates the government's attitude toward biomedical research. Special difficulties from the government-sponsored patient care programs of Medicare and Medi-Cal, in refusing to reimburse medical schools and their teaching hospitals for their actual costs of academic activities, are another ominous sign that we can no longer depend heavily on government to support our adademic programs.

It is clear to us in the School of Medicine that unless we begin to develop other sources of support, we will not be able to maintain the excellence

of our academic, research, and clinical missions. Nor is it logical to increase the intensity of a clinical practice in internal medicine since our clinical skills are high but our efforts in some areas may not be cost effective. Furthermore, any tilting of the delicate balance of distributions of time by our research-oriented faculty members would destroy our academic effectiveness, not improve our clinical skills or competence, and possibly reduce even further our flexible dollars for use in our academic programs. Increased clinical productivity at the expense of academic pursuits is no solution. Besides it is unrealistic to expect that our clinical activities will grow indefinitely. We are in a geographical area heavily supplied with doctors and a stable population growth with resultant fierce competition for fewer and fewer patients.

The problem of the Department of Medicine in trying to balance clinical and basic research activities is analogous to the plight of the Departments of Pediatrics and Psychiatry, and of all the basic science departments whose sources of research support are shrinking.

The second reason why collaboration with industry is now possible is the need to share talent. Industry attracts very capable economic, engineering and scientific planners to develop day-to-day strategy in laboratories. And it attracts many capable scientists. But it usually doesn't attract on a continuing basis scientists working on the forefront of basic clinical research. Nor, because of its economic orientation does it necessarily exploit the fundamental observations it makes if those observations have no obvious proprietary gain associated with them. Scientists who thrive on such findings usually seek a more appropriate home in an academic environment. These scientists, working on the forefront of advancing science with access to clinical facilities, could be of enormous assistance to industry in the transfer of new

pharmacologic developments and observations to biology and therapeutics. In addition, they can respond to new opportunities more readily than industrial scientific directors who are farther away from the bench or ward.

The clinical researchers, on the other hand, need access to industry not only for the development of their ideas into practical application, but access to areas of science not available in the medical school. These are organic, synthetic and analytical chemistry, development of toxicological testing, and sound businesslike decision making, to name but a few. Clearly these include areas for cooperation that can be critical to the future of industry and academe and apply to both academic clinicians and basic researchers.

AN INSTITUTE OF BIOLOGICAL AND CLINICAL INVESTIGATION

To develop the basis for long-term collaboration with industry, we propose to establish under the auspices of the Department of Medicine an Institute of Biological and Clinical Investigation. The Institute would be primarily the coordinating organization for the collaborative efforts of the faculty with industry. It would collect and distribute gifts for the primary purpose of developing young academicians, building academic research facilities, and initiating unconventional but academically promising projects in the Department of Medicine and other participating departments of the Medical School. The Institute would not be a separate entity from the University, but rather an interdisciplinary group functioning within and subject to the normal policies and practices of the University. As such, the University will have final responsibility and authority over the operations of the Institute. The Institute would have no monopoly on the kinds of activities with which it is involved, but will serve as a focal point for identifying and pursuing the opportunities available with respect to such activities.

Participation in the Institute eventually would be open to faculty in all departments whose members are willing to contribute their talents to specific projects and benefit by research collaboration with industry. Faculty participants will be governed by the bylaws and regulations of the Institute for work performed under specific contracts. In addition, faculty members selected for research collaboration with industry will agree to consider such a commitment a high priority as called for by the contract involved. To be successful, the project and faculty will have to be of such high caliber and so well matched that the results of the research collaboration will provide the basis for the best possible incentive for continuation of the effort.

The Institute will be directed by the Chairman of the Department of Medicine and a broadly based advisory committee which shall include at least one member of each of the departments participating in the work of the Institute. The members will be appointed on the basis of their scientific knowledge and judgment as well as their active interest in science and transfer of scientific results from the laboratory to practical application. The group of Chairman plus advisory group will be known as the Institute Governing Board. It will be the Governing Board's responsibility to define the policies and priorities of the Institute as well as govern the Institute in compliance with University policies and procedures in accordance with carefully spelled out responsibilities, reporting functions, and financial controls.

Aspects of Institute Structure

1. The Governing Board will have five members:
   a. In the first five years the Chairman of the Department of Medicine will be the Chairman of the Board; after that he/she will be a permanent member of the Board.

b. In the first year, the Chairman will select two members and the Department will elect the remaining two members of the Board; their terms will be two for one year and two for two years (one each elected).

c. After the first year, future members of the Board will be selected by "current" members. All selected in this manner will serve for two years. Selection should be cognizant of the divisions that are most active in the functions of the Institute.

d. After the first five years the Board will elect the Chairman of the Board from its own membership. He/she will serve a three-year term. Multiple terms are allowable.

e. Members of the Institute outside of the Department of Medicine can be elected to Board membership. Such a person can be one of the four selected. However, it may be considered more ideal if Medicine always has four "elected" members on the Board, in which case the number comprising the Board can be increased by two.

f. The Dean of the Medical School or his/her designee will be an ex-officio voting member of the Board.

2. The Board, in addition to concern with governance issues, will have the following responsibilities:

a. Review of the scientific merit of all research projects conducted under the auspices of the University which emanate from consulting activities under the auspices of

the Institute or are sponsored by funds derived from the Institute. The Board may appoint appropriate peer review committees of faculty in order to discharge this responsibility.

b. In consultation with the officers and relevant department chairmen, the Board shall approve disbursement of Institute funds for faculty, space and other development within the School.

c. The Board shall serve as an appeal body to consider and rule on requests of faculty for release from consulting obligations.

d. The Board shall oversee equitable distribution of consulting responsibilities among the participating faculty. That is, they should assist in providing appropriate consulting faculty for industrial concerns so that the needs of industry are met in the best possible way by the faculty.

e. The Board should set the priorities for the Institute. These should include primary and secondary goals:

Primary:

- o Development of new young faculty for replacement of retiring faculty or manning of new programatic needs in accordance with the School's five-year plans.
- o Development of research plans.
- o Purchases of common equipment.

Secondary:

- o Recognition of established academic programs where individuals are contributing significantly to activities of the Institute. This could be considered as "incentive" and allow divisions to "enhance" current academic programs by having access to funds.
- o Contact for general interaction of Institute with industry would include meeting with members of industry, general program presentations, negotiations or referrals to members within Institute. The latter case would be the identification of suitable consultants where expertise is sought by industry without requesting specific persons.
- o Monitoring performance of the Institute includes the entire effort as well as individual performance. This would include maintaining records of consultants activities, contracts awarded, quality of effort, and others as required.
- o Assist in making arrangements for further development of potential research projects where consultation has already occurred and additional work is needed before a formal research contract can be made.
- o Define specific policies pertaining to incentives with annual review. Constant redefinition of incentives will be required with passage of time and further experience. Incentives, once defined, may have to be adjusted accordingly to sustain maximum activity of the Institute.

- o Balanced view must be maintained. Although not characteristically a "function", but more an attitude, the Board must function with a "sense of balance" regarding departmental needs. The total needs of the Department must be considered against the specific needs of those contributing most to the Institute's goals. This issue must be addressed in a fair manner, but caution is warranted to prevent distortion of departmental goals.
- o Define policies regarding entry of individuals, groups, or departments outside of Medicine. This requires precise policies concerned with allocation of funds.

3. The Board shall be responsible for generating an annual or biennial review of the work of the Institute, and its relationship to academic missions which shall be conducted by a visiting committee consisting in part of individuals outside the Institute and outside the Medical School.

4. An oversight group will be established to insure the high quality of the science sponsored by the Institute, the equity of its operating procedures and the appropriateness of its use of funds for academic purposes. The group will be composed from three groups of members none of whom are at the time of their service participants in the Institute. From industry, one member; from academia outside of the Stanford system, one member; from academia inside of the Stanford system, three members. This group will meet once to twice a year for a period of two days to review the science and the decisions of the Board. They will have the right to access to all of the files of the Institute and to those of any of its participants. Their findings will be

submitted in written form to the Board with copies to the Executive Committee of the School of Medicine. Action for corrections of deficiencies will be made in collaboration with the offices of the Dean and Vice President for Medical Affairs.

Collaborative projects between industry and the Institute will involve basic research intended to generate new knowledge which will be performed pursuant to research contracts tailored for the particular projects. Proprietary interests of all collaborators (industry, the Institute, and the individual) will be addressed. Grievance procedures for settling disputes, and guarantees and mechanisms of governance will be an implicit part of any agreement, and incentives will be provided to all participants. These incentives will be devised so that they will not interfere with or divert academic priorities but will primarily extend and augment these priorities. As actual programs are undertaken for collaboration, their participants and peculiarities will determine the mechanisms by which they will be supported.

Funds received by the Institute shall be tax-exempt to Stanford University either as gifts from industry sponsors desirous of furthering the Institute's goals and objectives or, in those cases where a research collaboration occurs, as payment for the performance of basic scientific research.

Resources

Initially, collaborative projects with industry would begin using the faculty and resources of the Department of Medicine.

The Department has strong programs in cell biology, including mechanisms of immunity, steroid, lipid, polypeptide and amine receptorology, cell and membrane transport, and recombinant DNA research. In the clinical areas, the Department is a leader in the development (with our School of Engineering) of noninvasive cardiovascular diagnostic techniques.

In addition, it has strong programs related to cardiologic, immunologic, hypertensive, atherosclerotic, thromboembolic, infectious, renal, and rheumatic diseases, diabetes, calcium metabolism, and fundamental and clinical problems of the management of malignancies. Consultation would be available in areas of chemistry, endocrinology, metabolism, renal function, pulmonary therapy, lipids, antibiotics, interferon, antiviral and antineoplastic drugs, cardiovascular invasive and noninvasive techniques as well as clinical pharmacology and pro and eukaryotic cell biology.

As the initial collaborative attempts succeed and as we gain experience, we will enlist participation of other basic science departments in the work of the Institute. The Department of Medicine already maintains through joint appointments close ties with the Departments of Genetics, Immunology and Microbiology. Eventually we hope the scope of collaboration would expand as would the attractiveness of the Institute to both academic biologists and industry.

Collaboration is expected to be on a non-exclusive basis for either the Institute and its members or the industry. Projects that can be handled best by faculty in departments other than the Department of Medicine will be referred to them with greater ease than departmental barriers allow today.

Faculty Participation

1. Faculty participation in the work of the Institute is voluntary, but — like teaching, patient care, and other kinds of research — contributes to sustaining the academic mission of the Department.

2. Faculty adoption of the Institute by majority vote establishes the relationship between the Department and the Institute described above: that is, sanction by the majority as departmental policy makes the Institute one of the official functions of the Department.

3. Once a participating faculty member is called upon to consult with industry, he/she is expected to respond within a reasonable period of time. Flexibility in meeting this commitment is necessary, and will be recognized.

4. All participating faculty shall be available for consultation to a maximum of eight days annually.

5. Patterns and intensity of consultation within each division shall be structured so as to enhance and facilitate the overall academic responsibilities of the division, and shall not be permitted to place undue burdens on a few faculty for consultation or on non-consulting faculty for carrying extra work in order to allow some faculty to consult.

6. Consultation beyond the eight days per year shall be governed by the above considerations.

7. A participating faculty member desiring release from consulting obligations shall request that release from the Board and act in accordance with its decisions.

8. Faculty participation in the work of the Institute shall not be required for University recognition or promotion, which is judged on the basis of the quality of published research, teaching and clinical service.

9. Each division of the Department shall annually review faculty participation and report to the Department concerning its impact on the discharge of academic responsibilities by that division.

Academic Incentives

Academic incentives will develop in two ways. First, they will accrue through expanded departmental income, to be used for recruiting and developing young faculty. This in turn will enhance academic opportunities for present

faculty in the form of more individual time and increased opportunities for collaborating with new faculty. More laboratory space will be constructed. Secondly, it is quite possible that interactions will result among investigators across divisional, even departmental and school lines and with industrial scientists which will be unique and stimulating. Our academic provincialism could well be limiting and the Institute concept be beneficial.

Potential Conflicts of Interest

1. Work within the Institute shall be considered a regular academic responsibility. The intensity of this work and its timing shall be coordinated with other academic responsibilities in such a way that work of each division of the Department shall be discharged by the division as a whole, without compromise by excessive consultation on the part of one or more members. These relationships shall be overseen by division chiefs in conjunction with the department chairmen. If conflicts are not resolved, they shall be submitted to the Board.

2. All work done within the University or on University time other than the consultation shall be conducted with full disclosure of the general nature of the work. Issues related to procedures to ensure patentability of products of investigation have been recognized and surmounted by other research based institutes of the University and will serve as guides for the Board in setting up the Institute of Biological and Clinical Investigation.

3. Information obtained on specific consultations may be considered confidential. However faculty members shall not be limited in the number or types of consultations with other industrial concerns as the result of their work with an individual concern.

Information Collection for Review of Institute Function

The Institute shall keep a public record of:

1. All consultations by the faculty.
2. All research projects generated as a result of consultation.
3. Uses of all funds generated by the Institute.
4. All projects resulting in part or in whole from consultations and all publications resulting from work conducted or sponsored by the Institute.

The Collaborators and the Institute

The Institute will solicit gifts from industry and will use such gifts to perform its functions of the kind described below. No services will be rendered by the Institute in connection with such gifts. However, the Institute will serve as a clearinghouse for those corporate donors participating in the Institute. In this role, the Institute will assist the donor in finding appropriate consultants and making the necessary arrangements with them. By participating in the Institute, each faculty member has signified the willingness to consult with donors for up to eight days per year at a daily fee of $500 and expenses payable to the faculty member. Such consultations shall, where feasible, lead to the formulation of research collaborations between the Institute and donors, the terms of which shall be determined in each instance by an appropriate research contract between the University and the sponsor. Consultation will be ended when either the eights days are completed, when the consultation results in a contract for research collaboration on a project through the Institute, or when consultation is no longer needed.

Funds generated by the Institute will be distributed to the involved departments to support academic purposes and research.

The first priority will be to support the recruitment or research endeavors of developing faculty member (those with less than three years at Stanford).

The second priority will be to further the purposes of interdepartmental bridging projects as well as innovative research of established faculty which requires seed money to get started.

Funds could also be used for construction of research space.

THE VALUE OF THE PROJECT TO THE UNIVERSITY

Assets

1. Firm relationships with industry for a long period of time will be developed as opposed to ad hoc efforts of little value to the University and its purposes.

2. Depth and quality of scientific decision will be improved since not a single individual, but several experts can be called upon to work on a complex problem from many points of view.

3. The Institute's administrative structure, as well as individual research agreements guarantee an appropriate outcome of the agreement. The same type of academic and administrative attitudes with regard to accountability that relate to federal grants and contracts will apply to research agreements with industry.

4. Agreements will be those of equal partners. Industry, individual, and the University will not be subservient to each other. This approach is likely to encourage more academicians to overcome their reluctance in cooperating with industry.

5. Problems of technology transfer from University to industry can be addressed directly. Barriers will be removed. There will be less hesitation by industry to share with faculty basic scientific observations that have no proprietary benefit to industry. The result will be positive in both directions.

6. The Department of Medicine, initially forming the nucleus for this collaboration with industry, is small enough to organize it and be convincing in its commitment to carry it out.

7. The costs to be borne by industrial collaborators in this venture are small compared to other expenditures. For instance, in the case of Smith, Kline &French, the costs would amount to less than 1.0% of their research budget.

Areas of Particular Concern

1. The research role of the University is generation of knowledge for the good of society. Therefore, no arrangement with an external donor should be made that would compromise that goal (e.g., subordination to profit maximization).

2. Knowledge generation by the University requires openness concerning types of work done and public appraisal of the results of that work. Therefore, no arrangement with a client will be made that would impose secrecy on work done within the University.

3. The structures and functions of the Institute should be governed by explicit guidelines which are subject of periodic review. They have been mentioned.

4. It can be postulated that academic or industrial freedoms might be restricted by the proposed association. We believe such adversity could be

argued pro and con. The most likely outcome would be no restrictions on either side, at least fewer than are now imposed by governmental contracts and grants and some sources of restricted funds.

5. Collaboration between the University and industry arising out of the Institute shall be limited to those research projects the income from which will be tax-exempt to the University.

FUNDING

We propose to ask for a gift from any company interested in the proposed Institute. The gift pledge sought will be between $500,000 to $2,000,000 per year for a minimum of five years renewable after that at three-year intervals. We aim for collaboration with only a few companies and the faculty will provide no more time for consultations under their commitment to the Institute than listed above. These services will be divided according to the research interests of a particular industrial client that our faculty members are interested in, and who desires to tap the talents and expertise of our faculty who have commited to the Institute.

As an aggregate commitment, eight days of consultation per faculty member per year, and up to 400 days of consultation per year collectively will be available, with the requirement that individual faculty members invited to consult would be paid by industry $500 per day and expenses for formal consultative work. Once a particular industry and the faculty consultant have decided to pursue a project leading to a contract with the Institute, no further consultation fee will be required. Projects would be funded through an appropriate research contract or from an alternative appropriate source.

Proprietary rights would be negotiated as part of this contract. The precedent for these rights being divided between the creative parties already exists at Stanford. The details concerning proprietary rights still need to be worked out with the University administration but we see no substantive barriers to an equitable solution.

The Department of Medicine and all other participating departments will agree to submit to the Institute names of faculty members wishing to become involved, along with summaries of their research activities and a written commitment of their consulting time. If any faculty members are selected to consult or agree to work on a project for an industrial client, they will consider this involvement an important priority consistent, of course, with their academic commitments to the School and the University.

CONCLUSION

As a faculty of the Department of Medicine, we play many roles in efforts to fulfill our clinical, teaching, and research responsibilities. Common to all, however, is a continuing desire by each of us to see our work evolve into something ultimately beneficial to society. Initially that work might be a specific scientific result that enlarges a base of knowledge; it might be a technological accomplishment in the design of an important experiment; or it might be a bit of test data needed in a rush.

No matter what our ultimate hopes, we need mechanisms by which we can expedite the transfer of ideas from the University to industry to be manifested in practical application. Conversely, industry needs to draw in, from the outside, professors in the universitities who are advancing science to address critical questions in the competitive climate in which industry functions and to identify scientific opportunities, and viable programs and applications.

Clearly, the motivation for an experiment in innovative collaboration between the University and industry now exists.

More important, the proposed Institute for Biological and Clinical Investigation provides the first step in a series of actions that will be needed to develop alternate sources of support in order to decrease the dependence of academic departments on the uncertainty of federal funding.

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